
Transforming growth factor-alpha induces neurogenesis and behavioral improvement in a chronic stroke model.

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Authors: M Guerra-Crespo, D Gleason, A Sistos, T Toosky, I Solaroglu, J H Zhang, P J Bryant, J H Fallon

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Public Summary:

Scientific Abstract:

Transforming growth factor-alpha (TGFalpha) is a powerful endogenous mitogen and neurotrophic factor, which has previously been shown to induce a massive proliferative response in the brains of Parkinson's disease model rats injured by an acute neurotoxic lesion. We now show that TGFalpha can also produce a massive proliferative response in rat brains subjected to stroke caused by a middle cerebral artery occlusion (MCAO), even when the growth factor is administered as late as 4 weeks after injury. This combination of stimuli provokes DNA synthesis, shown by 5'-bromo-2-deoxyuridine incorporation, throughout the ependymal layer and subventricular zone (SVZ) of the forebrain during the 4 weeks of growth factor administration. The newly generated cells migrate preferentially along and ventral to the corpus callosum (CC) and external capsule to the site of the injury where many of them differentiate into several site-appropriate neuronal phenotypes in association with near complete (99%) behavioral recovery. We conclude that the injury response of endogenous neural stem cells as well as behavioral recovery can be significantly enhanced by application of TGFalpha, and that this approach represents a potential therapeutic strategy for chronic stroke and other neurological damage in human patients.

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